GENERAL MODEL FOR CALCULATION OF DRUG THERAPY COSTS

by

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FINAL READING APPROVAL

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ABSTRACT

This study developed a general model for the calculation of drug therapy costs for cost comparison of two or more therapeutically equivalent drugs. In order to identify all the costs of drug therapy, the drug use process was extensively studied and analyzed. A computer program was created to facilitate the calculations of drug therapy costs. Of importance, the study indicated that including only the acquisition cost of drug would provide values far below the actual costs, and that personnel costs can affect total drug costs substantially. Health care providers (pharmacists, physicians, hospital administrators and nurses) should include not only the acquisition cost of the drug, but also all other costs in their calculation of drug therapy.

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1 - INTRODUCTION

Health care costs have risen from 4.4% of the gross national product in 1950 to 10.6% in 1984 (1). Hospital expenditures in community hospitals alone rose from $14 per day in 1950 to $245 per day in 1980 (2). Because of the alarming rise in health-care costs, cost containment measures are crucial to hospital managers, physicians and pharmacists. With the implementation of diagnosis-related groups (DRG) in October 1983, cost containment in all aspects of hospital care has become necessary for hospitals to survive (3).

Drugs have not been exempted from the effects of health care cost containment. Although drugs and pharmaceuticals contribute on the average only 5% of hospital expenses (4), secondary to personnel costs, they are the most visible category of health care costs. It is also important to consider that about 6 to 8% of hospital costs are attributable to drug therapy costs (5).

One mechanism for containing drug costs is more rational, economical prescribing practices (6). However, the need for improved prescribing comes at a time when the selection of drugs has become difficult due to increasing numbers of agents. This is especially true for newer compounds such as the third-generation cephalosporins. In the literature, many examples exist where cheaper and older drugs can produce the same or even better results than the expensive newer ones (7,8,9,10,11).

Drugs, especially antibiotics, have a documented history of irrational uses which has unnecessarily increased the cost of drug therapy (12,13,14,15,16,17). Several studies have shown that substantial savings can be achieved through more rational drug therapy without compromising the patient (7,9,10,11,14,18).

When two or more drugs are therapeutically equivalent (considering that pharmaceutical considerations should not be ignored, such as palatability, dosage form and convenience), cost becomes the decisive factor in the choice of drug therapy. However, comparing only the acquisition costs of drugs will not serve the purpose well. All costs associated with drug therapy from the acquisition of a drug through to its administration to the patient and monitoring of the therapy should be included when comparing the costs of drugs. Before 1980 most researchers conducting cost comparisons of equivalent drug therapies considered only the acquisition cost of the drug when calculating the cost of drug therapy and did not include other costs (7, 8,17,18,19,20).

Statement of the problem and objectives of the study

Statement of the problem

If physicians and pharmacists were aware of all the costs involved in drug therapy, it still would be not feasible to expect them to calculate all the costs each time a decision concerning two therapeutically and pharmaceutically equivalent drugs was made. It is not easy to quickly identify the various costs involved in drug therapy because of the large variety . The calculation of drug therapy costs based on the acquisition cost of the drug will not furnish results that well represent total drug costs for comparison of two therapeutically equivalent drugs, though it seems the easiest and fastest way. From the drug use process, it is clear that the calculation of drug therapy costs involves a considerable number of calculations. Without a computerized software program it would certainly be discouraging to try to calculate total drug costs . Therefore, it is important that a generic computerized model, which includes all the costs for calculating drug therapies, be created to help health care providers (physicians and pharmacists) compare two or more therapeutically equivalent drug therapies.

Objectives of the study

The objectives of this study are to :

1) Identify the relevant costs (in dollar value) of total drug therapy for selected drugs at the University of Utah Hospital.

2) Create a general cost calculation model for the following pharmaceutical formulations : oral, injectable, topical and ophthalmic medications.

3) Write a computer program of the general cost calculation model that can be used for all drugs to calculate their total drug therapy costs.

4) Compare the difference between drug costs calculated from only the acquisition costs of the drug, to drug costs based on all costs calculated with the general cost calculation model.

Literature review

As early as 1972, researchers started to worry about the costs of drug therapy. Roberts and Visconti stated that irrational use of systemic antimicrobial drugs cost the patient, hospital and third party as much as $13,989.28 (76.8%) of the total annual $18,224.55 of antimicrobial drug costs (17) . However, they did not include the costs of preparation and administration in their calculations. It was mentioned that had this been done, higher costs for irrational and questionable therapy would have been found. Kunin et al. mentioned the high cost of antimicrobial drugs and made cost comparisons for several antimicrobials, but based the calculations on the acquisition costs only (6).

In a general way, most of the studies concerning costs of drug therapy consider the cost per gram of the drug, either to convey the high acquisition cost of the drug or to compare costs among therapeutically similar drug therapies (8,10,18,19,20,) . This is especially true for antibiotics such as the cephalosporins and the aminoglycosides. For instance, McGowan and Finland considered only the acquisition cost of the drug by measuring the costs (increase or decrease) in grams of the antibiotics used per year when they evaluated the usage of antibiotics in a general hospital (18). The average amount of ampicillin used was 7,127 g per year during 3 years (1966,1967,1968) when restricted; when not restricted, it raised to 57,600 g the next year, 1969. From 1969 to 1972 a mean use of 62,613 grams per year was found. During 1971, more than $250,000.00 was spent on antimicrobial agents and this amount was calculated based only on the cost per gram of the antibiotics.

The first mention of other costs besides acquisition costs was in 1976 when Klimek et al. compared the costs of two cephalosporins, cefazolin and cephalothin, considering the cost of administration (21). They concluded that the economic advantage of cefazolin was that it could be given intramuscularly, thus reducing costs involved with intravenous administration. Dudley and Barriere also mentioned that when doing cost comparisons among drugs one should consider dose frequency and route of administration (22). They determined that infrequent administration can often offset the greater acquisition cost of drugs with long serum half-lives.

In their calculation of cost reduction for an antibiotic control program, Craig et al. found that the average quarterly cost for all the antimicrobials was $16,358.00 for 1972 and that it could be reduced to $11,229.00 (31% reduction) during the 18 months of the control program (13). For cephalosporins, the reduction in the quarterly costs (1972) was from $4,719.00 to $1,014 during the control program, and this accounted for 72% of the decrease in total costs for antimicrobial drugs. Again, cost and saving calculations were based on the acquisition costs of the antibiotics. Maki and Schuna, when studying antimicrobial misuse, concluded that the average cost of an appropriate course of therapy was $55.30 and $84.45 for inappropriate therapy. These results were calculated considering the potential for overdose. For 14,650 patients in 1975, the cost of unnecessary antibiotics was $70,465.00 . This amount was based on the acquisition cost of the drug (14).

Noel and Paxinos reviewed cephalosporin use and performed a cost analysis. They studied the prescribing patterns for cephalosporin and restricted the use of cephalothin in a university hospital (20). Cost savings were studied over a 3-year period. Cephalosporin costs were calculated utilizing the amount of cephalosporin used, the cost per gram, and the number of doses taken by the patient. The restriction of cephalosporin use and the substitution of cephalothin for cefazolin resulted in a projected savings of over $5,500.00 for the fiscal year 1976-1977. Katz and Schalamowitz also studied the restricted use of cephalosporins during a 9-month surveillance period (8). From a total of 674 patients, they found that 92% received doses greater than those recommended in the literature. The dosage of cefazolin ranged from 1 gram every 4 hours to 1 gram every 6 hours while in the literature the recommended dosage is 250 to 500 mg every 8 hour or 500 mg to 1 gram for moderate to severe infections. Substantial savings were achieved with this program, a total of $33,196.00. The total amount of cephalosporin used decreased by 29%. These savings were calculated based on the quantity purchased, in grams.

When surveying cephalosporin use, Arthurson et al. calculated the cost of different courses of antibiotics and compared cephalosporin costs to penicillin costs (7). Drug costs were based only on invoice prices of the drugs. They found that the inappropriate use of cephalosporins would cost approximately $ 25.00 for the whole therapy, about twice that of more appropriate drugs.

It is interesting to mention that although Scheife et al. calculated the cost of cefoxitin sodium and clindamycin phosphate plus amikacin sulfate based only on the acquisition cost of the drugs, they concluded that the total cost of drug therapy can be influenced by other factors as personnel and material costs, besides drug cost (23). They emphasized that when those factors are present, they must be considered in cost analysis.

Paxinos et al. considered material and labor costs in their study of contamination rates and costs associated with the use of four intermittent intravenous infusion systems (24). They concluded that the major factor affecting the differences in costs is material costs and that labor costs accounted for only a small percentage of the total cost of the system and did not change the rank order costs established by material costs.

Only after 1980 did more studies begin to include other costs in addition to the acquisition cost of the drug . However, studies comparing the costs of two or more drug therapies based only on acquisition costs of the drugs can still be found. The study of Jewesson et al. (19) as well as that of Hayman and Sbravati (25) are good examples of this method of analysis. When auditing the use of cefoxitin at a 1,000-bed major teaching hospital in Vancouver, Jewesson et al. found that the cefoxitin use increased from 17.7% ($15,300.00) of the pharmacy's costs for cephalosporins during the first year of its availability to 47.7% ($60,707.00) during the second year. The cost was calculated by adding the total amount of cefoxitin used (in gram) multiplied by the cost per gram. In their calculations of cefoxitin costs, no other costs were considered. From Hayman and Sbravati's study of restricted use of cephalosporin and aminoglycoside during a 12 month-study, it was found that second-generation cephalosporin use decreased 52.2% (from 43,111 to 20,159 doses) with an increased use of 48.3% (35,319 to 52,414 doses) of first-generation cephalosporins. Tobramycin use was decreased by 75.9% and there was a 229% increase in gentamicin use. During the study period, the expenditure for injectable antibiotics was $193,172.06 less than during the year immediately precedings the restrictions. With the program, a decrease of $1.09 per patient day occurred in the total antibiotic cost . The cost savings were calculated using both (the first and the second generation of cephalosporins), and acquisition costs of the drug, but if other costs had been included, savings would have been higher.

When evaluating the use of antibiotic prophylaxis, Crossley and Gardner (1981) included the acquisition cost of the antibiotics, plus the cost of solutions and tubing in their estimation of antibiotics costs (12). According to Rapp et al. (1981), "the true cost of antibiotic therapy involves considerably more than the cost of the agent employed" (26) . They also mentioned that the costs ancillary to the antibiotic agent rarely have been studied. The ancillary costs they referred to were : 1) administration supplies; 2) laboratory monitoring; 3) pharmacy preparation time; and 4) nursing administration time. Their conclusions were that : a) the cost of the antimicrobial agent comprised only 50% of the total antibiotic therapy costs for single-agent therapy; b) 54% of total cost for combination therapy ; and c) that ancillary services occupied a fixed portion of costs and were related to the number of doses of antimicrobial agents.

Suzuki and Palham mentioned that studies about the cost-benefit of providing antimicrobial education and consultation failed to report the exact cost of providing education and consultation service and also the total material and personnel savings involved (27). For that reason, they determined drug costs by including the costs of the preparation and administration of drug therapy. They believed that important variables such as intravenous materials and personnel time (technicians, nurses and pharmacists) should be considered. The variables with injectable drugs were the acquisition costs of the drug, the diluent, the intravenous supplies, the intravenous piggyback seal and intravenous secondary set used by the nurse when administering the drug to the patient. They concluded that other costs should be present when calculating drug costs. Later, in his study comparing three different methods of preparing parenteral lidocaine solution for intravenous drip at Brigham and Women's hospital, Feldman determined that the volume control set system was more expensive than the syringe method when the cost of needed materials was included (28).

In comparing costs for reconstituted parenteral antibiotics, Tanner also included personnel and supply costs associated with preparation, dispensing and administration (29). Personnel costs were the costs associated with the pharmacist, the nurse and the technician. The supply costs that he considered relevant were : dextrose (5%, 50 ml), administration set, secondary set, syringe (10 ml), needle (18 gauge, 1.5 inch), swabs and sterile water (10 ml). He concluded that for maximization of cost containment, the route of administration should change from intravenous to intramuscular and that less frequent administration would provide cost savings. Cost savings would be due to decreased costs for drugs and supply changes, personnel time, inventory costs, waste problems, patient risk and length of hospitalization. He determined that the decreased number of administrations of first-generation and second-generation cephalosporins varies from $76.64 (25% reduction in doses administered) to $229.92 (75% reduction for the piggyback intravenous system and from $42.02 (25%) to $141.08 (75%) for the volume control intravenous set system. He also calculated the projected national cost savings for the first and second-generation cephalosporin based on the predicted antibiotic usage for 1983 . Cost savings would be from $ 62.2 million (25% reduction in doses administered with adjustment for no conversion to intramuscular or intravenous push administration) to $267.7 million (75% reduction).

Reilly et al. compared costs between two systems (syringe pump system and piggyback bottle system) for intermittent intravenous administration of small-volume injections, by separating the costs of both systems into fixed costs (small-volume container, label, container safety seal and transfer needle) and variable costs (secondary set, primary infusion set, with valve, adult and primary infusion set, plain, adult) (30). Personnel and material costs were included. They concluded that there was no difference in personnel costs between the two systems, but variations in time were required for individual tasks and, that the change from piggyback bottle system to syringe pump system would reduce the costs due to the reduction in material acquisition costs. Gouveia also stated that in providing drugs to patients, one should consider all costs of dispensing, distribution and administration (5).

Parr et al. did one of the best and most complete studies involving costs of drug therapy for injectable drugs (31). They calculated total costs for a therapeutic course including drug costs, supply costs and personnel costs for seven therapeutically equivalent intravenous antibiotic combinations for a simulated febrile neutropenic patient. A computerized model was developed including the various cost elements that contribute to the overall cost of preparing and administering those seven drugs. The laboratory costs for serum aminoglycoside blood concentration were also included. They concluded that the total costs of antibiotics were directly proportional to the acquisition costs of drugs and materials and that material costs represent from 72 to 94% of the total cost of therapy. The cost of a drug accounted for the major part of material costs ranging from 64% to 92% of the total costs. Personnel costs did not substantially affect total costs accounting for 6 to 30% of the total costs, and the percentage varied from drug to drug. The material costs, for instance, of gentamicin-ticarcillin was $654.08 (72%) and for monolactam-piperacillin was $2,393.16 (94%), while the personnel costs for the monolactam-piperacillin was $149.95 (6%), but for gentamicin-ticarcillin and cephapirin was $339.81 (30%). A shortcoming of the study was that they only considered the direct costs, thereby missing the indirect costs related to drug therapy, such as inventory storage costs, administrative personnel costs, utility bills, equipment depreciation and general overhead cost.

After mid-1980, other costs related to drug therapy were mentioned. First, it was Fant in his study of controversies and pitfalls in monitoring aminoglycoside therapy (32). He concluded that the total cost of drug therapy should include the cost of toxicity due to drug therapy (often very difficult to quantify) besides all costs of drug preparation, administration and laboratory monitoring . Second, Barriere mentioned about controversies in antimicrobial therapy (formulary decisions on third-generation cephalosporins) emphasized that other factors besides acquisition costs should be included in total costs of drug therapy (33,34). Barriere was one of the first to mention the need to include indirect costs. The factors he considered important and that contributed to the total economic impact of antimicrobial agents were : 1) acquisition costs; 2) preparation; 3) distribution; 4) administration; 5) control systems; 6) storage and inventory; 7) monitoring; and 8) use in ambulatory care (postdischarge ambulatory or home care) . Control systems, storage and inventory and use in ambulatory care were added to drug costs and these costs were classified as indirect costs.

This study attempted to measure the costs related to drug therapy.

2 - METHODS

The drug use process was extensively studied and analyzed to identify all the elements that could directly or indirectly contribute to drug costs. The factors considered relevant were classified as direct costs and indirect costs. The direct costs comprise supply costs, personnel costs and laboratory costs, while the indirect costs include all administrative costs such as utilities, office supplies, cleaning costs, storage, equipment depreciation and personnel indirectly related to drug therapy.

To quantify, in dollar value, the relevant costs in the drug use process, equations for direct and indirect costs were derived. The formulas were general in order not to be specific for the University of Utah hospital which was the site of the study .

The Director of Pharmacy at the University of Utah Hospital evaluated the identified relevant costs and helped to devise formulas to calculate the costs of drug therapy. This way relevant costs in the drug use process would not be missed.

There are four methods to calculate the acquisition cost of drugs: 1) FIFO; 2) LIFO; 3) average cost ; and 4) specific invoice price. LIFO, which means last in, first out, was used because it gives a more realistic price during inflationary periods. It is the last invoice price and would allow some loss recovery to counteract purchasing process problems. FIFO (first in, first out) could not be applied to drugs in a general way because it is very hard to find which was the price paid for a specific lot of the drug used. And the average cost for a drug is calculated from the average of the latest price and the last price. This method was not used because it was considered unappropriate . Also it is important to remember that it may cost more or even less to buy a drug at a specific moment when drug costs are being calculated. Last, the specific invoice price is usually used only for merchandise of great dollar value per dosage unit.

The cost for 24 hours of drug therapy was used to compare costs between drugs. First, the unit dose was used for the calculation of drug costs. The unit dose would be a tablet for oral drugs, a single dose in gram or milligram for injectable drugs and a single dose in drop or ml for liquids and ophthalmic drugs. The cost of one unit dose of the drug was calculated with the help of the computer program (created especially for this purpose) adding all the costs related to one dose of the drug. The result was multiplied by the number of doses per 24 hours to obtain total drug costs for 24 hours. Though a formula to calculate drug costs considering length of therapy in days was created in the computer program for this study, it was not used due to variations in length of stay for different patients.

The selection of the drugs for this study followed one or more of the following primary criteria : 1) invoice price; 2) dosing intervals; 3) preparation and monitoring; 4) adverse reactions; 5) route of administration; 6) length of therapy; and 7) formulary drug versus nonformulary drug. Comparisons were made for drugs differing in these criteria in order to determine the contribution of each criterion to the cost of drug therapy.

The head nurses of two different floors determined the materials used in drug administration and drug monitoring and served to document the laboratory tests ordered by the physician. Only the laboratory tests ordered specifically due to the drug administration were included in the calculation of drug therapy costs. However, the laboratory tests ordered routinely by the physicians that had connections with the drugs selected for this study were not considered in the calculation of total drug costs. For chlorthiazide and hydrochlorthiazide, the laboratory test included in the calculation of total drug costs was potassium and for gentamicin, it was gentamicin blood serum concentration .

The costs of the drugs, intravenous supplies and personnel were provided by the Director of Pharmacy and the Pharmacy Buyer. Prices of material costs which were not available to pharmacy personnel were obtained from the Hospital Storeroom supervisor. The acquisition costs of all materials were from 1985 inventory. All personnel wages used in the calculations of drug costs were average wages and included fringe benefits, with the exception of the pharmacy intern who does not receive benefits. Because the tasks performed in providing drug therapy took less than an hour and the wages were calculated on an hourly basis, it was necessary to recalculate wages from an hour to a minute scale. The change was performed in processing sections, 1040, 1050, and 1060 of the computer program.

All materials that could not be directly allocated to a unit dose and that would provide a dollar value too small to be included as relevant costs were considered as indirect costs. For instance, during the preparation of injectable drugs, sterile gloves and extension sets were also used, but the technician prepared several unit doses of different drugs with the same pair of gloves (the same situation happened with extension sets). It was difficult to estimate the percentage of the glove cost used and therefore allocate to each unit dose of the drug , and that is why it was classified as an indirect cost.

The time personnel (technician, pharmacist and nurse) spent with the preparation, the administration, and the monitoring of injectable drugs were extracted from the study of Parr et al. study (31). The reasons for employing these data were : 1) the main objective of their study was to calculate total costs of drug therapy and so it was the objective of this study ; 2) it is by far one of the best designed and most complete studies in drug cost calculations; and 3) it had a large number of observations of the time nurses, technicians, and pharmacists spent performing a task . The number of observations varied from 60 to 100.

In this study, it was considered that nurses were involved in drug administration and monitoring; therefore the time the nurse spent in drug preparation was considered zero. The time the nurse spent in drug administration and monitoring was 5.25 minutes per dose for the injectable drug. The time the clinical pharmacist spent monitoring the injectable drug (16 minutes) was divided by number of doses per 24 hours because it was assumed that it took 16 minutes for drug monitoring daily (31) . For the calculations of total drug costs in this study, it was considered that the pharmacist was involved in drug preparation and drug monitoring and did not have any relationship with drug administration .

The time personnel spent in the administration and the monitoring of oral and topical drugs was obtained from Locklear's study (35). Those data were used because : 1) the project was performed at the University of Utah Hospital; 2) it was determined the time nurses spend in administering oral and topical drug; and 3) it was a well conducted study .

No data reflecting the time technicians spent on repackaging unit doses from a bulk container for oral drugs (tablets) were found in the literature. Therefore, a stopwatch method was used to collect data at the pharmacy of the University of Utah Hospital. The observation of packing the unit dose tablets by the technician started from the moment he checked the drugs that should be packed in unit dose and stopped after he labeled the drugs. The process of packing tablets in unit dose was observed for variable times (from 1 to 3 hours) for 10 days.

All other costs reflected costs to the hospital and not to the patient, including laboratory costs. The laboratory costs were furnished by ARUP (Associated Regional and University Pathologists, Inc.), an independent clinical laboratory that performs all laboratory tests for the University of Utah Hospital.

A computer program was created for the general model to facilitate and make faster the calculation of drug costs, to provide a more efficient and precise way to calculate costs related to drug therapy, and to furnish consistency (so all the drug costs calculations would be performed the same way). Also, this program made the calculation of drug costs more available to physicians, pharmacists, nurses, health care providers and other lay people interested in drug costs calculations. With the assistance of a computer programmer, the program was written in the Basic language. Basic was used because it was considered the best language for this type of calculation, and also for the possibility that Basic can be used in other computers. To validate the program function and its accuracy, costs of one of the selected drugs (cefoperazone) were calculated using a calculator. The results furnished by the computer program were compared with the ones obtained from the calculator. The computer program was designed using the formulas devised to calculate the costs and was created to be as general as possible, so it could be used for all pharmaceutical formulations and by other hospitals. Mathematical rounding was done on the results of total drug costs in the computer program.

The calculation of drug costs based only on the acquisition costs of the drug was done with the computer program for doses over a 24 hour period. The same process was performed with the calculation of total costs of drug therapy. The costs of the materials used in the administration of injectable drugs were calculated by taking the acquisition cost of the materials divided by the number of doses per 24 hours. If the material was used for 48 hours, its acquisition cost was divided by the number of doses per 48 hours. The materials used were : 1) dextrose 5% 500 ml (24 hours); 2) intravenous set with injection sites (48 hours); and 3) Harvard microbore extension set (48 hours). For solutions that were used in drug preparation, the process was that if 10 ml of the injection solution was used in drug preparation, then the cost for only 10 ml was calculated.

To calculate the cost difference for the 16 selected drugs, the cost of drugs (based on the acquisition cost only) was subtracted from total drug costs calculated using the computer model. To obtain the percentage, the difference between total drug costs and acquisition costs of drug was divided by cost of drugs and multiplied by 100. Percentage was used because the great variation in the acquisition costs of the selected drugs would not allow comparison .

Limitations of the study

When studying the costs of drug therapy, the first important factor to remember is that the patient may be taking more than one medication. This means that the nurse may be administering other drugs to the patient at the same time, besides the one being studied. If this happened, it would certainly affect the time the nurse spent administering the drug. For this project it was assumed that the patient took only one medication at the time of the drug administration which may or may not be the case.

Another factor limiting this study is assuming that the most frequently recommended daily dosage was the standard one. For instance, for chlorthiazide, the dosage was considered as 1 tablet per day, but it may have happened that the patient had 2 tablets per day, or even had 1 tablet every 48 hours . When calculating the costs of drugs, it is essential to consider the number of doses per 24 hours .

To facilitate calculations, the indirect costs of drugs were considered as a percentage of the total direct cost. The number used (22.70 %) and assigned by the accounting department to pharmacy reflected how indirect costs would affect the costs of the drug considering pharmacy as a department of the hospital. The number used in the calculation of total drug costs may be more or less than the actual number. Indirect costs such as telephone bills, utilities bills, cleaning supplies, office supplies, storage, inventory, equipment depreciation, intangible costs and personnel indirectly related to the drug therapy (as housekeepers) were allocated as an estimation. If one had tried to calculate the costs of each indirect cost it would have taken not only a very long time but the results would also be represented as very insignificant values. Therefore, the results would still be an estimation and less precise than the percentage used . Another aspect restricting the use of indirect costs as a percentage of direct costs is that indirect costs are proportional to the dollar value of direct cost. If direct costs were high, indirect costs were high too. That is, if the acquisition cost of a drug was high, indirect cost would be high, even if most of the indirect costs were (or should be) constant regardless of direct costs. But this shortcoming could be compensated by considering the fact that the more expensive the acquisition cost of the drug , the less capital the hospital has to use in profitable investments.

One of the most important factors not introduced in the calculation of drug therapy is the cost of adverse reactions which are costly not only to the patient but also to the hospital . The patient may suffer undesirable side effects of the drug and take other medications to suppress adverse reactions of the drug. It is not unreasonable to assume that the patient may even have to be hospitalized for a longer period of time. The latter would be certainly costly to the patient and to the hospital.

The estimation of costs of the adverse drug reactions is a not an easy task. Adverse reactions vary from patient to patient. Some patients may be much more sensitive to the side effects of a drug than others, and the costs would most likely be different for different patients. So, with one single drug there are different adverse reaction costs for different patients. Considering the number of drugs used in a hospital, years of study would be necessary just to get an estimation of costs of adverse reactions for all drugs. These may be the reasons why not many data about costs of adverse reactions were available in the literature. In a study performed by a pharmaceutical company (Hoescht), estimations of the costs of adverse reactions for different antibiotics were performed . These data were not used in this study because: 1) it was a study done for only some antibiotics; and 2) it was necessary to make extrapolations of the data as only antibiotics were included . Unfortunately, conclusive data about costs of adverse drug reactions cannot be found, even though they are often speculated about.

Another factor limiting this study was the data used for injectable drugs . Most of the data on the time personnel (nurse, technician and pharmacist) spent performing an activity were extracted from a study that was not done at the University Hospital. These data came from a hospital located in another geographic area with different techniques to prepare, and to administer injectable drugs. The main reason for using the data was because the study was well done.

Another factor that should be mentioned is laboratory tests. According to the head nurse there were routine laboratory tests that physicians ordered for the patient which may or may not be related to the drug the patient was taking. Not including laboratory tests related to drug administration may have changed total drug costs and reduced the results in dollar value. If more laboratory costs were included, total drug costs would have been higher than the results obtained in this study .

Last , it is essential to mention that the drugs used to test the computer model were not chosen at random, but selected out of convenience. This process was done because it was necessary to include injectable, oral, topical and ophthalmic drugs.

3 - RESULTS

The drug therapy process was studied and six major steps were derived from it. The first step is the prescription for the drug which is generally the responsability of the physician. After being prescribed, the drug is purchased by the Pharmacy department, and this second step is called acquisition. Many times drugs are purchased in multiple dose, or must be prepared before being administered to the patient, so this third phase was denominated as preparation. The drug is prepared in the Pharmacy and then it must be delivered to the patient, so this step was named delivery. After being delivered, the drug will be administered to the patient by the nurse, and this step was considered as administration. Finally, after receiving the drug, the patient will be monitored. It is important to observe that not all drugs have to go through all these steps, and for some drugs, one or two steps mentioned above do not exist. Each step was analyzed to find the relevant factors contributing to the total costs of drug therapy. This study of the drug use process generated the following results:

The prescription is the first phase of drug therapy and it provides the following information: 1) number of doses per 24 hours ; 2) route of administration; and 3) length of therapy.

The acquisition is the second phase of drug therapy and consists of : 1) the acquisition cost of the drug ; 2) the wages of the buyer that are proportional to the time spent ordering the drug; 3) the wages of the receiving clerk that are proportional to the time the receiving clerk spends receiving the drug; 4) the wages of the storekeeper that are proportional to the time the storekeeper spends to put drug on the shelves; and 5) administrative costs.

Administrative costs included : 1) materials such as office supplies and cleaning supplies; 2) utility bills -- electricity, gas and water ; 3) telephone bill, like long distance calls; 4) equipment depreciation, e.g., typing machine, xerox machine, computer; 5) administrative salaries, e.g., secretary, computer programmer, supervisor, assistant director of pharmacy; 6) costs related to messengers; 7) department cost -- general overhead; 8) drug wastage due to drug preparation and expiration of the drug; and 9) taxes (this item was not included for the University Hospital because it is a nonprofit hospital). Also, it is important to remember two constant costs : 1) drugs in stock which represent capital that could be in the bank gaining interest; and 2) inventory storage costs (the personnel required to perform the yearly inventory and the shelve space the drugs need, both costing money to the hospital). The department costs are all the costs that are indirectly related to drug therapy such as providing journals, sending pharmacists to conferences, meetings, hiring personnel (turnover), etc. These are indirect costs. The direct cost for acquisition cost phase is the invoice price for a unit dose of the drug.

Drug preparation is the third phase of drug therapy . The factors included in this phase are :

1) the cost associated with the pharmacist's wages per hour proportional to the time spent with drug preparation.

2) the cost associated with the technician wages per hour proportional to the time spent in drug preparation.

3) the cost associated with the nurse's wages per hour proportional to the time spent in drug administration.

4) the materials used for drug preparation.

5) the cost of the drug considering drug wastage during the preparation of a unit dose.

6) the monthly depreciation of the equipment used in the preparation of the drug such as unit dose tablet packaging machines and laminar flow cabinets.

Drug delivery is the fourth phase of drug therapy. This step included the cost of the messenger (messenger's wages) and the depreciation of the delivery cart if it is being used. But in emergency cases, only a few doses are delivered, so the delivery cart is not necessary.

Drug administration is the fifth step of drug therapy and includes : 1) the personnel (nurse); 2) the materials; and 3) the depreciation of equipment.

Drug monitoring is the sixth phase of drug therapy and is composed of: 1) the costs of the personnel monitoring the drug (the nurse and/or the pharmacist); and 2) the cost of laboratory tests.

To calculate the cost of drug therapy at the University of Utah Hospital, the following items were considered as the relevant costs : 1) the acquisition cost of the drug; 2) the percentage of the drug lost during preparation of one unit dose of the drug; 3) the materials to prepare the drug; 4) the materials to administer the drug; 5) the materials to monitor the drug ; 6) the technician wages; 7) the time the technician spends on drug preparation ; 8) the nurse's wages; 9) the time the nurse spends in drug preparation and drug administration ; 10) the pharmacist wages; 11) the time the pharmacist spends on drug preparation and drug monitoring ; 12) laboratory tests ; and 13) indirect costs as a percentage of the total direct cost.

The drug delivery phase was considered as indirect costs because: 1) many doses of different drugs were delivered and the number of the delivered doses varied considerably; and 2) the person who delivers drugs varied and could be anyone of the following group: nurse, technician or pharmacist.

A general model for the calculation of the costs with formulas for the oral, injectable, topical and ophthalmic drugs was created. The calculation of drug costs was based on 24-hours of drug therapy and the elements considered were : 1) the cost for one dose of the drug; and 2) the number of doses per 24 hours .

The main formula (number 1) needed to calculate the total drug costs consists of five separate equations and each equation will be described. The first equation is:

$$Cd = CD/D + CS/D + CP/D + CI/D + CL/D \quad (1)$$

where : 1) Cd is the cost for one dose of the drug

2) CD/D is acquisition cost of one dose of the drug

3) CS/D is the cost of supplies per dose

4) CP/D is the cost of personnel per dose

5) CI/D is the indirect costs per dose

6) CL/D is the cost of the laboratory tests per dose.

As mentioned before, when comparing the costs of two therapeutically equivalent drugs, it is better and easier to compare the cost of drug therapy for 24 hours than for the total length of the therapy, because the length of therapy may vary from patient to patient . Therefore, an equation was developed for this purpose . The equation for a 24 hour drug therapy is :

$$CDd = Cd \times Nd \quad (2)$$

where : 1) CDd is the cost of a 24 hour drug therapy; 2) Cd is the cost of one dose of the drug; and 3) Nd is the number of doses per 24 hours.

For cases where the costs of the whole length of drug therapy can vary from 1 to n, an equation was created:

$$CT = CDd \times NDT \quad (3)$$

where : 1) CT is the total cost of the drug therapy ; 2) NDT is the length of drug therapy; and 3) CDd is as above (2).

Each component of the equation (1) is described below. The first equation is for drug cost per dose (CD/D), and is represented by :

$$CD/D = CPC1/NDC \quad (4)$$

where : 1) CPC1 is the cost of the drug considering the amount of drug wasted in drug preparation; and 2) NDC is the number of doses in one container. The formula to include drug wastage is :

$$CPC1 = CPC + WPR \quad (5)$$

where : 1) CPC is the acquisition cost of the drug without considering drug wastage, and 2) WPR is the percentage of the drug lost during the preparation of one dose of the drug. The equation for WPR is :

$$WPR = X\ CPC \quad (6)$$

where: X is the percentage of the indirect cost.

When the drug is in the multiple dose container, the number of doses per container must be known. If there is only one dose in the container, then CD = CPC (where CD is the acquisition cost of the drug), and the dollar value would be the invoice price of the drug.

The next equation is for the cost of supplies per dose (CS/D) and is represented as :

$$CS/D = MPR + MAD + MMO \quad (7)$$

where : 1) MPR is all the materials used for the preparation of a unit dose. To calculate it, all the costs of the materials used in drug preparation were added; 2) MAD is all the materials used for the administration of a unit dose. To calculate it, the same procedure was used for MPR; and 3) MMO is all the materials utilized in the administration of a unit dose. To calculate it, use the same procedure as for MPR .

The equation CP/D is the one that represents the cost of the personnel per dose. This equation involves technicians, nurses and pharmacists. Physicians are not included because patients must pay physician's fees separately . The equation for personnel costs is :

$$CP/D = CT + CN + CPH \quad (8)$$

where :

1) CT is the cost associated with the technician, and its equation is :

$CT = STe \times (tPRTe)$ (9)

where :

1) STe is the technician wages/hour ; and 2) tPRTe is the time the technician spent on drug preparation .

2) CN is the cost associated with the nurse. The nurse can be involved in the preparation, administration and monitoring of the drug. The equation for CN is :

$CN = SN \times (tPRN + tADN + tMN)$ (10)

where : 1) SN is the nurse wages/hour ; 2) tPRN is the time the nurse spent in drug preparation; 3) tADN is the time the nurse spent in drug administration and; 4) tMN is the time the nurse spent in drug monitoring.

3) CPH is the cost associated with the pharmacist, which can be involved in drug preparation, drug administration and drug monitoring. CPH's equation is :

$CPH = SPH \times (tPRPH + tADPH + tMPH)$ (11)

where : 1) SPH is the pharmacist wages per hour; 2) tPRPH is the time the pharmacist spent on drug preparation ; 3) tADPH is the time the pharmacist spent on drug administration ; and 4) tMPH is the time the pharmacist spent on drug monitoring .

The equation that represents all indirect costs and intangible costs per dose of drug is the equation number 12 . These costs are the department's general overhead costs, costs associated with the buyer, store keeper, receiving clerk, and other personnel indirectly involved with the drug acquisition phase (housekeeping and maintenance personnel, administration personnel) drug wastage due to expiration, utility bills, equipment depreciation (all the equipment related directly or indirectly to the drug therapy), inventory costs, administrative personnel wages, messenger, etc. It is difficult to name all indirect costs, especially intangible costs. For the pharmacy as a department of the University hospital the formula that represents the allocation of these indirect costs is :

$CI = X\ DC$ (12)

where: 1) CI is the indirect cost ; 2) X is the percentage assigned by accounting department to pharmacy; and 3) DC is the direct costs.

The last equation represents the cost of laboratory tests per dose (CL/D) . The number of the tests performed during the therapy were added and divided by either the number of doses or days depending on what was needed : the total cost of the drug per dose or the drug cost per day. This step was necessary because laboratory tests are performed on a daily basis and only a single test may be required for the entire therapy. The equation for the cost of laboratory tests per day is :

$$CL = Lt1 + Lt2 + Lt3 + \ldots\ldots \quad (13)$$

where Lt1, Lt2, Lt3 are the prices of different types of laboratory tests. If a test was performed more than once a day, the following equation was used:

$$Lt(n) = lt \times Nlt \quad (\text{ n varies from 0 to infinite }) \quad (14)$$

where : 1) lt is the price of one laboratory test, and 2) Nlt is the number of the laboratory tests in 24 hours.

To test the software, eight pairs of drugs were selected from oral, injectable and topical drugs. The first set of drugs was gentamicin 80 mg and cefoperazone 1.0 gram. The criteria used to select these drugs were : 1) invoice price; 2) dosing intervals; 3) preparation ; 4) monitoring ; and 5) adverse reactions (especially for gentamicin).

The second set of drugs was Actifed®[a] and Drixoral®[b] . This pair was selected because : 1) they are prescribed for cold symptoms ; 2) they are oral drugs (tablets) ; 3) they have different invoice prices; 4) they have different dosing intervals; and 5) Drixoral® needs to be packed in unit dose, while Actifed® comes prepacked in unit dose.

The main criterion utilized to choose the third set of drugs, gentamicin ophthalmic ointment and gentamicin solution ophthalmic, was the need to have a pair of topical

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[a] Actifed is tripolidine hydrochloride 2.5 mg and pseudoephedrine hydrochloride 60 mg , and it is manufactured by Burroughs Wellcome Co.

[b]Drixoral is dextropheniramine maleate and pseudoephedrine sulfate, and is manufactured by Schering Corporation.

drugs. Their different ways of administration and different dosing intervals were also considered.

Ampicillin 500 mg capsules and ampicillin 1.0 gram intravenous was the fourth set of drugs selected . The main reason for choosing this set was to compare different dosage forms of ampicillin. Different preparation and invoice prices were other factors taken into account .

The fifth set of drugs was cimetidine 300 mg and ranitidine 150 mg. The criteria to select this pair were : 1) both are oral drugs; 2) both are prescribed for gastric ulcer; 3) they have different invoice prices; 4) they have different dosing intervals; and 5) they have different lengths of therapy.

Darvocet-N 100®[c] versus propoxyphene hydrochloride 65 mg plus acetaminophen 1.0 gram was selected as the sixth pair of drugs. The main reason for choosing these drugs was to compare the costs of formulary drugs to the costs of nonformulary drugs. The same criteria were utilized for the seventh pair of drugs, chlorthiazide 500 mg and hydrochlorthiazide 50 mg.

The last pair of drugs was leucovorin calcium 25 mg versus folinic acid 25 mg . The main criterion for their selection was to compare costs of drugs prepared in the hospital pharmacy and drug product purchased from the manufacturer and or wholesaler.

The materials used in the preparation of injectable drugs were alcohol swabs, solutions of dextrose 5% 500 ml, solutions of dextrose 5% 1000 ml, labels for the syringe, transfer needles, solutions of sodium chloride 0.45% 1000 ml, solutions of sterile water 500 ml and both 10 ml and 60 ml-syringes and syringe caps.

The available data to test the general computerized model for the calculation of drug costs were :

1. The acquisition cost of the drugs is shown in Table 1.

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[c]Darvocet N-100 ® is propoxyphene napsylate and acetaminophen, and it is manufactured by Eli Lilly and Company.

Table 1 - Acquisition cost per container of the 16 selected drugs

Drug	Cost		
Acetaminophen 1 g	5000 tablets	@	$ 28.99
Actifed®	1000 tablets	@	$ 14.59
Ampicillin 500mg	500 tablet	@	$ 35.50
Ampicillin 1 g	1 g	@	$ 0.65
Cefoperazone	2 g	@	$ 18.40
Cimetidine 300mg	100 tablets	@	$ 32.49
Chlorthiazide 500mg	100 tablets	@	$ 9.57
Darvocet N-100®	500 tablets	@	$ 47.15
Drixoral®	100 tablets	@	$ 18.49
Folinic acid 25mg	1 capsule	@	$ 4.05
Gentamicin injectable	800mg/20ml	@	$ 1.65
Gentamicin ophth. sol.	1 bottle 1% 5ml	@	$ 0.92
Gentamicin ophth. oint.	1 tube 3 g	@	$ 1.54
Hydrochlorthiazide 5mg	1000 tablets	@	$ 3.99
Leucovorin 25mg	25 tablets	@	$599.17
Propoxyphene 65mg	500 tablets	@	$ 38.60
Ranitidine 150mg	60 tablets	@	$ 40.33

2. The percentage of drug wastage was considered zero for oral and intravenous drugs.

3. The acquisition costs of the supplies are shown in Table 2 .

4. The preparation time, administration time and monitoring time spent by personnel for injectable, oral and topical drugs and the wages of the personnel are displayed in Table 3 .

5. The indirect costs for the pharmacy department (the percentage of X, see formula 12) at the University of Utah Hospital were considered as 22.70 % of the total direct costs (with the exception of laboratory tests). The original number assigned was 20.7%, but for the unidentified costs another 2% was assigned by the Director of Pharmacy .

6. The prices of the laboratory tests are in Table 4.

7. Table 5 shows the drugs with their route of administration and doses per 24 hours.

8. The cost of drug therapy was calculated based on the acquisition cost of the drug only and on all other relevant costs. The results are shown in Table 6. The differences between costs calculated from the purchase price and the cost calculated from all costs for the eight sets of drugs were compared.

Table 2 - Cost of the supplies used in drug therapy

Supplies	Unit Cost
Alcohol swab	$ 0.0175
Plastic cup for tablets	$ 0.0080
Dextrose 5% 500ml	$ 0.6500
Dextrose 5% 1000ml	$ 0.8300
Harvard microbore extension set	$ 3.3730
IV set 2 injection sites	$ 0.6920
Label for syringe	$ 0.0060
Transfer needle	$ 0.0400
Sodium chloride 0.45% 1000ml	$ 0.8500
Sterile water 500ml	$ 0.7700
Sterilized syringe 10ml	$ 0.3700
Sterilized syringe 60ml	$ 0.5500
Syringe cap	$ 0.0500

Table 3 - Personnel time (in minutes) and wages per hour

Personnel	Time (inj.)	Time (oral)	Time (topical)	Salary
Pharmacist	0.91	–	–	$ 17.80
Pharm. monit.	16.00	–	–	$ 17.80
Nurse	5.25	1.03	1.33	$ 14.08
Technician	3.16	0.29	–	$ 8.19

Table 4 - Costs of laboratory tests

Laboratory test	Price p/test
Potassium	$ 5.00
Gentamicin blood level	$30.00

Table 5 - The 16 selected drugs, their route of administration and number of doses per 24 hours

Drug	Administration Route	Dose p/24 hours
Actifed®	oral	4
Ampicillin 500mg	oral	4
Ampicillin 1 g	IV	4
Cefoperazone 1 g	IV	2
Cimetidine 300mg	oral	4
Chlorthiazide 500mg	oral	1
Darvocet N-100®	oral	6
Drixoral®	oral	2
Folinic Acid 25mg	oral	4
Gentamicin 80mg	IV	3
Gentamicin oph.sol.[a]	topical	4
Gentamicin oph.oint.[a]	topical	2
Hydrochlorthiazide[c]	oral	1
Leucovorin 25mg	oral	4
Propoxyphene [b]	oral	6
Ranitidine 150mg	oral	2

a) administration of the drug to one eye only.

b) propoxyphene + acetaminophen 1 g

Table 6 - Difference between the calculation of the cost of drug therapy based on acquisition costs and the calculation of costs based on all costs for 24 hours

Drug	Actual inventory cost	Calculated cost	Cost difference
Actifed®	$ 0.06	$ 2.59	$ 2.53 (4217%)[a]
Ampicillin 500mg	$ 0.28	$ 1.57	$ 1.29 (461%)
Ampicillin 1 g	$ 2.60	$ 25.91	$ 23.31 (897%)
Cefoperazone 1 g	$ 18.40	$ 37.80	$ 19.40 (105%)
Cimetidine 300mg	$ 1.30	$ 2.82	$ 1.52 (117%)
Chlorthiazide 500mg	$ 0.10	$ 1.14	$ 1.04 (1,040%)
Darvocet N-100®	$ 0.57	$ 2.53	$ 1.96 (344%)
Drixoral®	$ 0.38	$ 1.19	$ 0.81 (213%)
Folinic Acid 25mg	$ 16.20	$ 21.10	$ 4.90 (30%)
Gentamicin 80mg	$ 0.49	$ 21.91	$ 21.42 (4,371%)
Gentamicin oph.sol.[b]	$ 0.04	$ 1.58	$ 1.54 (3,850%)
Gentamicin oph.oint.[b]	$ 0.31	$ 1.14	$ 0.83 (268%)
Hydrochlorthiazide	$ 0.004	$ 1.03	$ 1.026 (26,650%)
Leucovorin 25mg	$ 95.87	$118.85	$ 22.98 (24%)
Propoxyphene [c]	$ 0.50	$ 2.45	$ 1.95 (390%)
Ranitidine 150mg	$ 1.34	$ 2.26	$ 0.92 (69%)

a) cost difference was also calculated in percentage due to different acquisition costs of drugs

b) administration of the drug to one eye only

c) propoxyphene + acetaminophen 1 g

9. The costs of the personnel, materials, laboratory and indirect costs were calculated for all drugs, and the results are shown on Table 7.

The computer program to calculate the cost of drug therapy was written in the Basic language and was based on the 14 formulas described above. This program has three sections : the input section, the processing section and the output section. The input section gathers data. The processing section calculates material costs, personnel costs and laboratory costs. Finally, the output section gives the results. The software calculates the cost of drug therapy as the cost per dose, the cost per 24 hours and the cost per therapy. It also gives the percentage of: 1) material costs versus total costs; 2) personnel costs versus total costs; and 3) drug costs versus material costs. The program will answer questions such as the contribution of personnel costs and material costs (in percentage). The program is shown in its full details in the Appendix .

Table 7 - Personnel costs, material costs (including drug costs) and indirect costs related to total costs in percentage

Drug	Material costs/ Total Costs	Personnel costs/ Total Costs	Indirect costs/ Total Costs
Actifed®	7.08%	74.53%	18.39%
Ampicillin 500mg	19.87%	61.42%	18.71%
Ampicillin 1 g	33.33%	48.17%	18.50%
Cefoperazone 1 g	58.72%	22.79%	18.49%
Cimetidine 300mg	47.23%	34.28%	18.49%
Chlorthiazide 500mg	9.10%	21.24%	69.66%
Darvocet-N100®	24.43%	57.26%	18.31%
Drixoral®	34.29%	47.38%	18.33%
Folinic Acid 25mg	76.93%	4.58%	18.49%
Gentamicin 80mg	22.19%	48.13%	29.68%
Gentamicin oph.sol.	2.53%	74.17%	23.30%
Gentamicin oph.oint	27.19%	54.51%	18.30%
Hydrochlorthiazide	1.16%	23.57%	75.27%
Leucovorin 25mg	80.69%	0.81%	18.50%
Propoxyphene[a]	23.84%	59.17%	16.99%
Ranitidine 150mg	60.00%	21.37%	18.63%

a) propoxyphene and acetaminophen 1 g

4 - DISCUSSION

The computer program is open to changes either by deleting formulas or by adding equations, if necessary. Some people may argue that the created formulas and the computer program were too general, but it was designed this way to permit flexibility and let other hospitals besides the University hospital use them. This program calculates the costs of drug therapy in a simple and accessible way, and can be easily implanted in personal computers. It also allows anyone interested in drug therapy costs to calculate them provided that data (material costs, personnel costs and laboratory costs) are available.

For Actifed® and Drixoral®, interesting results were found. If drug costs were based on acquisition costs only, Actifed® ($0.06) was six times cheaper than Drixoral® ($0.38). But when all other costs were included, Drixoral® costs ($ 1.19) were half of Actifed's® ($2.59). These results were explained by the difference between Actifed's® dosage (4 doses per 24 hours) and Drixoral®'s dosage (2 doses per 24 hours). Drixoral® costs more than Actifed® and this was shown by higher percentage of material costs/total costs, for Actifed 's® percentage of material costs/total costs was 7.08% while Drixoral® had a ratio of 34.29%.

Before discussing personnel costs related to drug therapy costs , it is essential to emphasize that personnel costs are fixed costs and not variable costs . For example, a nurse receives a fixed salary per year. However, the time spent on the administration of the drug to the patient varies with the number of doses and the form (oral, topical or injectable drug) of the medication. For instance, the nurse usually spends more time with an injectable drug than with an oral drug. However, the percentage of personnel costs in relation to total drug therapy costs varies according to the acquisition cost of the drug, the supplies and laboratory costs.

On the calculation of drug therapy costs, when considering the acquisition costs of cimetidine and ranitidine only , cimetidine 300 mg ($1.30 per day) was cheaper than ranitidine 150 mg ($1.34 see Table 1.6) . Nevertheless, when all other costs were included, cimetidine was more expensive ($ 2.82 per day) than ranitidine ($2.26 per day). Material costs/total costs for cimetidine were lower (47.23%) than for ranitidine (60.00%). But the percentage of personnel costs/total costs were higher for cimetidine (34.28%) than for ranitidine (21. 37%). These results can be explained by the higher number of doses per day of cimetidine (4 per 24 hours for cimetidine versus 2 times a day for ranitidine) which increases the personnel and material costs.

The number of doses per 24 hours for ampicillin 500 mg (oral) and ampicillin 1.0 g (injectable intravenous) was the same (4 per 24 hours). However, drug costs were quite different. For drug costs based on the acquisition costs only, ampicillin 500 mg ($0.28) was nine times cheaper than ampicillin 1.0 g ($2.60). With all costs included, the difference was enhanced, for ampicillin 500 mg ($1.57) was 16 times cheaper than ampicillin 1.0 gram ($25.91). Since ampicillin 1.0 gram was administered intravenously, this medication required more material and personnel time for its preparation and administration. These differences were clearly shown on the percentage of material costs/total costs and personnel costs/material costs. . For ampicillin 1.0 gram, the ratio material costs/total costs was 33.33% and for ampicillin 500 mg was 19.87%. Due to the lower acquisition costs of ampicillin 500 mg , the percentage of personnel costs/total costs was higher for ampicillin 500 mg (61.42%) than for ampicillin 1.0 gram (48.17%), though the actual personnel costs were higher for ampicillin 1.0 gram (the nurse and the pharmacist spent more time with the patient).

Hydrochlorthiazide was the least expensive drug among the 16 selected drugs. An immense difference, 132.650%, between the costs calculated on the acquisition costs of the drug only (\$0.004) and the costs based on all other costs (\$5.31) was found. This enormous difference was mainly caused by laboratory costs of potassium test which accounted for 94.16% of total costs. Due to the low acquisition cost of hydrochlorthiazide, the cost of the potassium test seemed extremely high (\$ 5.00) when compared to hydrochlorthiazide acquisition costs (\$0.004). The same argument is true for chlorthiazide, the laboratory test accounted for 92.25% of the total costs. The high cost of laboratory tests suppressed by far material costs and personnel costs and this is true for both drugs. For chlorthiazide the material costs/total costs ratio was 1.99% and for hydrochlorthiazide was 0.24% . The personnel costs/total costs ratio for both drugs is also very low. For chlorthiazide it was 4.46% and for hydrochlorthiazide 4.55%. From this set of drugs, it is possible to assume that laboratory costs can change drastically the ratio of material costs per total costs and the ratio of personnel costs per total costs, especially when the acquisition costs of the drug are very cheap.

With laboratory tests present for gentamicin 80 mg, the ratio of laboratory cost/total costs is 29.68%, for chlorthiazide is 93.55%, and for hydrochlorthiazide is 95.21%, then other costs (indirect costs plus laboratory costs) were higher than if these tests were absent. When the material costs ratio was low (chlorthiazide 1.99% and hydrochlorthiazide 0.24%), and laboratory costs were much higher than the acquisition cost of the drug, then other costs accounted for the largest part of total costs. For all other drugs that did not include laboratory tests, other costs varied from 16.99% to 23.30%.

From this study, it is clear that as the number of doses of a drug per 24 hours increases, material costs, personnel costs, and total drug costs also increase. A common widely used argument is that it does not matter the number of doses administered by nurses to the patient per day, because they are paid to work for fixed hours and they are in the hospital . However, it is worth remembering that saving nursing time in drug administration, the saved time can be used to perform other tasks (new programs) and also that nurses will be able to give patients better care and have more patients to care without changing the quality of service (this will increase productivity).

From Table 6, it is possible to infer that the difference among the drug costs calculated based on the acquisition cost only and the drug costs on all costs was quite significant. This difference varied from 24% to 132,650%. When the acquisition cost of an oral drug is high, the difference is not so tremendous (24%) as in the case of leucovorin 25 mg ($ 95.85 per 24 hours). But if the acquisition cost of the drug is very low as for hydrochlorthiazide 50 mg ($ 0.004 per 24 hours), the difference is huge (132,650%). For Pharmacy and Therapeutics Committees, physicians and other health care providers when they have to make a decision between drugs and when cost is the main factor in their selection of two or more therapeutically similar drugs, it is essential to bear in mind that besides the acquisition cost of the drug, all other costs should be included in the calculation of drug therapy costs.

Oral drugs seemed to present higher percentage of personnel costs per total costs. It was very interesting to observe that cheaper acquisition costs of a drug can produce higher personnel costs/total costs ratio . But one must remember that percentage is being discussed here and that personnel costs are fixed costs. When the rate of material costs per total costs was high, personnel costs/total costs rate was low. Several studies emphasized that personnel costs do not account heavily on drug costs (24,30, 31). For instance, Paxinos et al. concluded that personnel costs do not change the rank cost order established by material costs (24) and Reilly et al. determined that there was no difference in personnel costs when they compared piggyback bottle system and syringe pump system (30). Parr et al. also found that personnel costs do not affect total costs substantially, accounting from 6 to 30 % of the total costs (31). But, it is fundamental to mention that in those studies the drugs studied were presented in the injectable form, and that a great portion of the drugs were the ones considered expensive. This project included all pharmaceutical formulations, inexpensive drugs and expensive drugs and these could be the reason of the great variance in personnel costs (0.81% to 74.53%). For personnel costs, Actifed® had higher personnel costs/total costs ratio (74.53%) than Drixoral® due to the higher number of doses per 24 hours, while Drixoral® had a lower number , two doses compared to four doses of Actifed® (47.38%). So for Actifed®, personnel costs/total costs were 74.53%, accounting for the majority of total costs. It was noticeable that for all selected drugs when material costs/total costs ratio was higher for one drug than for the other, personnel costs/total costs were lower for the drug with higher material costs. For the gentamicin ophthalmic solution, material cost was 2.53% and for the gentamicin ophthalmic ointment it was 27.19%. However, personnel cost for gentamicin Ophthalmic solution was 74.17% whereas it was 54.51% for gentamicin ophthalmic ointment. The results of above mentioned studies (24,30,31) concluded that personnel costs do not account heavily on total costs as said previously, but this study found that personnel costs can account for the majority of drug therapy costs (up to 74.53%). The cheaper the material costs, the higher the personnel costs, and this relationship was valid for two therapeutically similar drugs when laboratory costs were not included in the costs of one of the drugs.

5 - CONCLUSION AND FURTHER RESEARCH

This study indicates that to calculate the costs of drug therapy based on the acquisition cost would provide values far below the actual costs. Health care providers, physicians, pharmacists, and other people interested in drug costs should be aware that besides the acquisition cost of the drug, other costs should be included in the calculation of drug therapy costs. Realizing that there is a low probability of including all costs in the calculation of drug therapy costs, it is essential to include as many costs as can be identified and keep in mind that the obtained results may still not reflect the actual total.

If it had been possible to include the costs of adverse reactions to the calculation of drug therapy, bigger differences between the cost of drug therapy based on acquisition costs and based on all costs would have been found in some cases. As mentioned before, adverse reactions have not been studied . There is a long way to go, as it will be necessary to find the best way to quantify and calculate adverse reactions costs for different drugs considering individual patient variations . This is an area that certainly deserves more attention and studies.

APPENDIX

COMPUTER PROGRAM

```
100 REM INPUT SECTION
103 INPUT "How many days will the therapy last?",NT
106 INPUT "How many doses will be given per day?,NDPD
110 INPUT "What is the price of the drug (invoice price)?",CPC
120 INPUT "How may doses are in one container?",ND
125 WPR = 0
130 IF ND = 1 GOTO 150
140 INPUT "How many different materials are used in preparing the  drug?" , N
160 MPR = 0
170 IF N = 0 GOTO 230
180 FOR I = 1 TO N
190 PRINT "What is the price per dose for material number ";I;"?"
200 INPUT MN
210 MPR = MPR + MN
220 NEXT I
230 INPUT "How many different materials are used in administering the drug? ,N
240 MAD = 0
250 IF N = 0 GOTO 310
260 FOR I = 1 TO N
270 PRINT "What is the price per dose for material number ";I;"?"
```

```
280 INPUT MN
290 MAD = MAD + MN
300 NEXT I
310 IF MMO = 0 GOTO 390
340 FOR I = 1 TO N
350 PRINT "What is the price per dose for material number ";I;"?"
360 INPUT MN
370 MMO = MMO + MN
380 NEXT I
390 INPUT "What is the technician hourly wage?",ST
400 INPUT "How many minutes does the technician spend on drug preparation?, TTP
410 INPUT "How many minutes does the technician spend on drug monitoring?",TTM
420 INPUT "What is the nurse hourly wages?",SN
430 INPUT "How many minutes does the nurse spend in administering the drug?",TNA
440 INPUT "How many minutes does the nurse spend on drug monitoring?",TNM
450 INPUT "What is the pharmacist hourly wage?",SP
460 INPUT "How many minutes does the pharmacist spend on drug preparation?",TPP
470 INPUT "How many minutes does the pharmacist spend in administering the
drug?",TPA
480 INPUT "How many minutes does the pharmacist spend on drug monitoring?",TPM
490 INPUT "How many different laboratory tests will be done during the therapy?",N
500 CL = 0
510 IF N = 0 GOTO 570
520 FOR I = 1 TO N
530 PRINT "What is the cost of lab test number";I;?"
540 INPUT CLN
545 INPUT "How many times will the test be done during the therapy?",M
```

```
550 CL = CL + CLN * M

560 NEXT I

570 INPUT "What is the indirect cost as a percentage of the total direct  cost?", CIP

1000 REM PROCESSING SECTION

1010 CPC1 = CPC * (1 + WPR/100)

1020 CD = CPC1/ND

1030 CS = MPR + MAD + MM0

1032 TCS = CS * NDPD

1034 TTCS = TCS * NT

1036 CM = CD + CS

1039 TCM = CM * NDPD

1040 CT = ST * (TTP + TTM) / 60

1050 CN = SN * (TNA + TNM) / 60

1060 CPH = SP * (TPP + TPA + TPM) / 60

1070 CP = CT + CN + CPH

1072 TCP = CP * NDPD

1074 TTCP = TCP * NT

1080 REM COMPUTE THE TOTAL COST

1090 TC = (CD + CS + CP) * NDPD * NT

1100 TC = TC * (1 + CIP/100) + CL

1110 CPD = TC/NT

1112 WTCP =  TCP/CPD * 100

1120 CPDS = CPD/NDPD

1130 TC = INT(TC * 100 + .5) / 100

1140 CPD = INT(CPD * 100 + .5) / 100

1150 CPDS = INT(CPDS * 100 + .5) / 100

1160 CL = INT(CL * 100 + .5)
```

```
2000 REM OUTPUT SECTION
2010 PRINT "The total cost of the therapy is $";TC
2020 PRINT "The cost per day is $";CPD
2030 PRINT "The cost per dose is $";CPDS
2040 PRINT "The cost of the laboratory tests is $";CL
2050 PRINT "The cost of the material per dose is $";CS
2052 PRINT "The cost of the material per day is $";TCS
2054 PRINT "The cost of the material per therapy is $";TTCS
2060 PRINT "The cost of the personnel per dose is $";CP
2062 PRINT "The cost of the personnel per day is $";TCP
2064 PRINT "The cost of the personnel per therapy is $";TTCP
2070 PRINT "The percentage of the personnel/therapy is";WTCP
2080 PRINT "The percentage of the drug/material is"WCD
2090 PRINT
2100 PRINT
3000 END
```

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